DATA EVALUATION RECORD

1-2-BENZISOTHIAZOLIN-3-ONE, 2-BUTYL-
(DENSIL DG Fungicide)

STUDY TYPES: **Product Identity and Composition (OPPTS 830.1550)**
Description of Beginning Materials (OPPTS 830.1600)
Description of Production Process (OPPTS 830.1620)
Discussion of Formation of Impurities (OPPTS 830.1670)
Preliminary Analysis, Certified Limits (OPPTS 830.1700, 830.1750)
Enforcement Analytical Method (OPPTS 830.1800)
Physical and Chemical Characteristics (OPPTS 830.6302-830.7950)

MRIDs 45380901, 45380902, 45380903, 45380904, 45380905, 45380906, 45380907

+454071-01

Prepared for
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Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
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Toxicology and Risk Analysis Section
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Action No. K293

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1,2-Benzisothiazolin-3-one, 2-butyl-
MRIDs 45380901, 45380902, 45380903,
45380904, 45380905, 45380906, and 45380907

Product Identity and Composition (OPPTS 830.1550)
Description of Beginning Materials (OPPTS 830.1600)
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EPA Reviewer: Nancy Whyte, Ph.D. Date: July 17, 2001

EPA Work Assignment Manager: Bonaventure Akinlosotu, Ph.D., Antimicrobials Division (9510C) Date: _____

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CASE NO.: 070296

P.C. CODES:

Ingredients	P.C. Code	CAS No.
Active Ingredients		
Vanquish Technical N-Butyl-1,2-Benzisothiazolin-3-one	098951	4299-07-04
Inerts		
[redacted]		
Impurities		
[redacted]		

Chemical names are taken from the CSF for DENSIL Fungicide

Impurities don't need codes. NA

DP BARCODE: D274448

SUBMISSION: S596267

MRID Nos.: 45380901, 45380902, 45380903, 45380904, 45380905, 45380906, 45380907

TEST MATERIAL: 1-2-Benzisothiazolin-3-one, 2-butyl- (EPA Reg. No. 72674-EG)
(CAS No. 4299-07-4)

SYNONYMS: none found

STUDY/REPORT NUMBERS:

MRID 45380901 – Laboratory Project ID: VPG-1
MRID 45380902 – Laboratory Project ID: VPG-3
MRID 45380903 – Laboratory Project ID: VPG-2
MRID 45380904 – Laboratory Project ID: VPG-4
MRID 45380905 – ASG Project ID: Project 702416, RD 012459B
MRID 45380906 – ASG Project ID: Project 702416, RD 012557B
MRID 45380907 – ASG Project ID: Project 702416

SPONSOR: Avecia, Inc., P.O. Box 15457, 1405 Foulk Road, Wilmington, Delaware, 19850-5457

TESTING FACILITIES:

MRID 45380901 – Avecia, Inc., 1405 Foulk Road, Wilmington, Delaware, 19850-5457
MRID 45380902 – Avecia, Inc., 1405 Foulk Road, Wilmington, Delaware, 19850-5457
MRID 45380903 – Avecia, Inc., 1405 Foulk Road, Wilmington, Delaware, 19850-5457
MRID 45380904 – Avecia, Inc., 1405 Foulk Road, Wilmington, Delaware, 19850-5457
MRID 45380905 – ZENECA Specialities: (a) Analytical Sciences Group (ASG) Specialities Research Centre, Hexagon House, Blackley, Manchester, M9 8ZS, UK and (b) Fire and Explosions Units, Process Hazards Section, ZENECA Process Technology, Blackley, Manchester, M9 8ZS, UK

MRID 45380906 – ZENECA Specialities: Analytical Sciences Group (ASG) Specialities Research Centre, Hexagon House, Blackley, Manchester, M9 8ZS, UK
MRID 45380907 – ZENECA Specialities: Analytical Sciences Group (ASG) Specialities Research Centre, Hexagon House, Blackley, Manchester, M9 8ZS, UK

TITLE OF REPORTS:

MRID 45380901 – DENSIL DG Fungicide Confidential Statement of Formula
MRID 45380902 – DENSIL DG Fungicide Manufacturing Process
MRID 45380903 – DENSIL DG Fungicide: Discussion of the Formation of Impurities
MRID 45380904 – DENSIL DG Fungicide: Preliminary Analysis and Analytical Method
MRID 45380905 – DS 6039: Physical Chemical Characterisitics Data to Support EPA Registration. Project 702416
MRID 45380906 – DS 6039: Storage Stability Testing to Support EPA Registration. ANNEX to Project 702416

MRID 45380907 – DENSIL DG Fungicide: 12 Month Storage Stability Study Report at 0-Time

AUTHORS:

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REPORTS ISSUED:

MRID 45380901 – March 27, 2001
MRID 45380902 – March 27, 2001
MRID 45380903 – March 27, 2001
MRID 45380904 – March 27, 2001
MRID 45380905 – August 1997
MRID 45380906 – July 1998
MRID 45380907 – August 1997

EXECUTIVE SUMMARY: The product identity and composition, beginning materials, production process, potential impurities, preliminary analysis, enforcement analytical method, and physical and chemical characteristics of DENSIL DG fungicide, EPA Reg. No. 72674-EA, are addressed in MRIDs 45380901, 45380902, 45380903, 45380904, 45380905, 45380906, and 45380907; a CSF, some administrative material; and the product label. DENSIL DG Fungicide is to be used in metal cutting, metal lubricating, metal cooling, metal cleaning, and metalworking fluids. It contains the active ingredient N-butyl-1,2-benzisothiazolin-3-one (EPA Reg. No. 72674-EG) with a percentage by weight of 46.02 for the source material, VANQUISH technical (97.8% a.i.), with certified limits of 44.5 – 48.0%. The CSF does not list the % a.i. in the end-use product, which would be 45.01% with limits of 43.66 – 46.36%. The label gives the % a.i. as 45%. [redacted] Data regarding the preliminary analysis of DENSIL DG Fungicide was limited to one batch. OPPTS 830.1700 requires the preliminary analysis of five batches of the product. The production process for DENSIL DG Fungicide involves [redacted]

[redacted] The enforcement analytical method used is high performance liquid chromatography (HPLC). The physical and chemical characteristics of DENSIL DG Fungicide were addressed adequately with the exception of corrosion characteristics. No specific information is provided regarding the commercial packaging used for DENSIL DG Fungicide.

Classification of studies:

Product Identity and Composition and Certified Limits (OPPTS 830.1550 and 830.1750) – **Unacceptable**, but upgradeable when the CSF is corrected to include the % a.i. in the source material and the % nominal and limits for the a.i. and not just the source material. Typographical errors should also be corrected. The label should be made consistent with the CSF with regard to the number of significant figures for the a.i. and the inerts.
Description of Beginning Materials (OPPTS 830.1600) – **Acceptable**
Description of Prodution Process (OPPTS 830.1620) – **Acceptable**
Discussion of Formation of Impurities (OPPTS 830.1670) – **Acceptable**
Preliminary Analysis (OPPTS 830.1700) – **Unacceptable**, but upgradeable if preliminary analysis data for a total of five batches of DENSIL DG Fungicide are provided.
Enforcement Analytical Method (OPPTS 830.1800) – **Acceptable**
Physical and Chemical Characteristics (OPPTS 830.6302-830.7950) – **Acceptable** except for corrosion characteristics.

COMPLIANCE: Signed and dated Data Confidentiality statements and Good Laboratory Practice (GLP) statements were provided for MRIDs 45380901, 45380902, 45380903, 45380904, 45380905, 45380906, and 45380907. Quality Assurance statements were provided for MRIDs 45380905 and 45380906.

A. PRODUCT IDENTITY AND COMPOSITION (OPPTS 830.1550)

The components of the formulation of DENSIL DG Fungicide are provided in Table 1 below. The CSF should be corrected to include the % a.i. in the source material (i.e., 97.8% a.i.) and the % nominal and limits for the a.i. and not just the source material. Typographical errors should also be corrected. The label should be made consistent with the CSF with regard to the number of significant figures for the a.i. and the inerts. The source of the active ingredient is the registrant.

does not affect nominal

second place is not significant! often can be ignored as a difference

TABLE 1. Components in Formulation of DENSIL DG Fungicide					
Name of component	CAS No.	Percentage by weight	Certified Limits (% by weight)		Purpose in formulation
			Upper Limit	Lower Limit	
VANQUISH Technical (97.8% a.i.)* N-Butyl-1,2-Benzisothiazolin-3-one	4299-07-04	46.02*	48.0*	44.5*	active ingredient
[redacted]					
* - the % a.i. is 45.01% nominal with limits of 43.66–46.36%					

Data obtained from CSF for DENSIL DG Fungicide

B. DESCRIPTION OF BEGINNING MATERIALS AND FORMULATION PROCESS (OPPTS 830.1600 AND OPPTS 830.1650)

The materials used in an example 1000 lb formulation of DENSIL DG Fungicide include 460.2 lbs of VANQUISH Technical (97.8% N-butyl-1,2-benzisothiazolin-3-one) and [redacted] [It should be noted that on the CSF, the amount of VANQUISH Technical (97.8% N-butyl-1,2-benzisothiazolin-3-one) used in a 1000 lb formulation is given as 460.02 lbs and the % by weight is given as 46.02%. However, on p. 4 of 19 in MRID 45380902, it is indicated that 460.2 lbs of this component is used in the formulation. The registrant should correct this discrepancy.] The CSF states that [redacted]

The manufacturing process for DENSIL DG Fungicide involves [redacted]

Material Safety Data Sheets (MSDSs) are provided in MRID 45380902 for each of the beginning materials.

C. DISCUSSION OF FORMATION OF IMPURITIES (OPPTS 830.1670)

DENSIL DG Fungicide is formulated by [redacted]

D. PRELIMINARY ANALYSIS (OPPTS 830.1700)

On p. 4 of 4 of MRID 45380904, the following statement is made: "Since the product is not yet registered for marketed [sic] at the present time, large scale product batch samples are not available for analysis. Therefore, the study reports analysis of a small scale batch. These data and the results from the final report on storage stability should be sufficient to support registration." Information regarding the analysis of one batch of DENSL DG Fungicide is made available in MRID 45380906 (p. 10 of 11). The analytical method used was HPLC analyses utilizing a HP1090M instrument with a Spherisorb S5 ODS-1 column. The % w/w for the active ingredient (N-butyl-1,2-benzisothiazolin-3-one) and one of the impurities [redacted] were within the certified limits as specified on the CSF. However, OPPTS 830.1700 requires the preliminary analysis of five batches of the product. The registrant should provide preliminary analysis data for an additional four batches.

E. CERTIFIED LIMITS (OPPTS 830.1750)

The certified limits for the components of the formulation for DENSIL DG Fungicide, as listed on the CSF, are provided in Table 1 above. The CSF should provide the certified limits based on % a.i., not just based on the source material.

F. ENFORCEMENT ANALYTICAL METHOD (OPPTS 830.1800)

The enforcement analytical method used is HPLC utilizing an HP 1090 Chemstation Liquid Chromatograph with a Spherisorb S5 ODS-1 column and a UV detector. The sample and standard solutions were examined and the areas under the appropriate peaks were used to determine the concentration of the active ingredient and the levels of impurities present in the test substance by the external standard procedure. A chromatogram was provided on p. 17 of 29 in MRID 45380905.

G. PHYSICAL AND CHEMICAL CHARACTERISTICS (OPPTS 830.6302-830.7950)

The following properties of the end-use product and methods used to calculate them were provided in MRIDs 45380905 and 45380906.

Color (830.6302): brown (at ambient temperatures and under "normal" lighting)

Physical State (830.6303): viscous liquid (at ambient temperature)

Odor (830.6304): no obvious odor

Density (830.7300): 1.09 at 20°C

pH (830.7000): 7.7 (2.5% v/v solution in 40:60 1,4-dioxane:water)

Oxidation/Reduction: Chemical Incompatibility (830.6314): The MSDS for VANQUISH Technical, the source of the active ingredient, states that it is incompatible with alkaline materials, mild steel, oxidizing agents, and acids (p. 8 of 19, MRID 45380902).

Flammability (830.6315): The flash point of DENSIL DG Fungicide is 109 ± 4°C (228 ± 7°F). The test was carried out according to ASTM D93-90 for Pensky-Martens closed cup testing.

Storage stability (830.6317): An accelerated storage stability test was carried out for DENSIL DG Fungicide in glass containers at 54 ± 2°C over a period of two weeks. HPLC analyses utilizing a HP1090M instrument with a Spherisorb S5 ODS-1 column indicate an initial concentration of active ingredient (%w/w ± standard deviation) of 45.2 (± 0.3). After two weeks, the concentration of active ingredient (%w/w) was determined to be 45.2 (± 0.3). As stated in the results provided in MRID 45380905 (p. 28 of 29), there was no significant active ingredient degradation over the test time period and, according to the CIPAC Handbook (Volume 1 MT 46), this indicates an ambient shelf life of at least two years. No significant change in the impurity profile was noted. Chromatograms of the test substance

before and after two weeks of storage at 54 ± 2°C were provided in MRID 45380905 (p. 29 of 29).

A 12-month storage stability test was also conducted. The test substance was stored in high density polyethylene containers in the dark under ambient conditions. (It should be noted that the registrant does not specifically state that the commercial packaging material for DENSIL DG Fungicide is made of high density polyethylene.) The ambient temperature was monitored and ranged from approximately 15°C to approximately 27°C over the 12 months. The analytical method used was HPLC analyses utilizing a HP1090M instrument with a Spherisorb S5 ODS-1 column. The test results are provided in Table 2 below. No significant changes were observed, other than minor differences in retention times and resolution expected in the application of the methodology (i.e., column aging and minor differences in eluent composition due to the analyses being carried out on different dates). Chromatograms are provided in MRID 45380906 (p. 11 of 11). No change in appearance of the sample was noted over the 12-month period of the test. No information is provided regarding any changes in the containers used for this 12-month study.

TABLE 2. Results of 12-month storage stability tests of DENSIL DG Fungicide

Component	Initial % w/w*	Final % w/w*
N-Butyl-1,2-Benzisothiazolin-3-one (active ingredient)	45.2 (± 0.3)	45.1 (± 0.3)
2,2'-bis(butylcarbamoyl)diphenyl-disulphide (impurity)	0.15	0.15
Component 1 (impurity)**	0.05	0.05
Component 3 (impurity)**	0.15	0.15
Component 4 (impurity)**	0.05	0.05
Component 6 (impurity)**	0.15	0.05

*– all results corrected to nearest 0.05
**– no specific name was provided for these components (impurities)

Data obtained from p. 10 of 11, MRID 45380906

Viscosity (830.7100): The viscosity of DENSIL DG Fungicide was measured using a BOHLIN VOR Rheometer. This product was found to be Newtonian in character with a viscosity of 41.3 milliPascal Seconds at 25°C.

Corrosion characteristics (830.6320): Weighed de-greased test coupons were incubated with the test substance for four weeks in the absence of light at 50 ± 1°C. At the end of the test, the coupons were weighed and inspected visually for signs of corrosion. The coupons tested were aluminum, carbon steel, stainless steel 304, stainless steel 306, and polypropylene.

After four weeks, no weight loss was found in any of the test coupons and the coupons showed no evidence of corrosion. However, an average weight gain of 0.5% was observed for the polypropylene coupons. No information was provided regarding corrosion characteristics for any time period longer than four weeks. The manufacturing process for DENSIL DG Fungicide indicates that the final product is placed in drums. No specific information is provided regarding the commercial packaging used for DENSIL DG Fungicide.

H. DISCUSSION

The product identity and composition, beginning materials, production process, potential impurities, preliminary analysis, enforcement analytical method, and physical and chemical characteristics of DENSIL DG fungicide, EPA Reg. No. 72674-EA, are addressed in MRIDs 45380901, 45380902, 45380903, 45380904, 45380905, 45380906, and 45380907; a CSF, some administrative material; and the product label. DENSIL DG Fungicide is to be used in metal cutting, metal lubricating, metal cooling, metal cleaning, and metalworking fluids. It contains the active ingredient N-butyl-1,2-benzisothiazolin-3-one (EPA Reg. No. 72674-EG) with a percentage by weight of 46.02 for the source material, VANQUISH technical (97.8% a.i.), with certified limits of 44.5 – 48.0%. The CSF does not list the % a.i. in the end-use product, which would be 45.01% with limits of 43.66 – 46.36%. The label gives the % a.i. as 45%. [redacted] Data regarding the preliminary analysis of DENSIL DG Fungicide was limited to one batch. OPPTS 830.1700 requires the preliminary analysis of five batches of the product. The production process for DENSIL DG Fungicide involves [redacted] The enforcement analytical method used is HPLC utilizing an HP 1090 Chemstation Liquid Chromatograph with a Spherisorb S5 ODS-1 column and a UV detector. The physical and chemical characteristics of DENSIL DG Fungicide were addressed adequately with the exception of corrosion characteristics. No information was provided regarding corrosion characteristics for any time period longer than four weeks and no specific information is provided regarding the commercial packaging used for DENSIL DG Fungicide. In addition to the 12-month storage stability test conducted utilizing high density polyethylene containers, an accelerated storage stability test was carried out using glass containers at 54 ± 2°C over a period of two weeks.

Classification of studies:

Product Identity and Composition and Certified Limits (OPPTS 830.1550 and 830.1750) – **Unacceptable**, but upgradeable when the CSF is corrected to include the % a.i. in the source material and the % nominal and limits for the a.i. and not just the source material. Typographical errors should also be corrected. The label should be made consistent with the CSF with regard to the number of significant figures for the a.i. and the inerts.
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Description of Prodution Process (OPPTS 830.1620) – **Acceptable**
Discussion of Formation of Impurities (OPPTS 830.1670) – **Acceptable**
Preliminary Analysis (OPPTS 830.1700) – **Unacceptable**, but upgradeable if preliminary analysis data for a total of five batches of DENSIL DG Fungicide are provided.
Enforcement Analytical Method (OPPTS 830.1800) – **Acceptable**
Physical and Chemical Characteristics (OPPTS 830.6302-830.7950) – **Acceptable** except for corrosion characteristics.

I. STUDY DEFICIENCIES

The CSF does not provide the fact that VANQUISH Technical contains 97.8% a.i., and does not provide the nominal concentration or certified limits based on the % a.i. The product label should match the significant figures provided on the CSF. It should be noted that on the CSF, the amount of VANQUISH Technical (97.8% N-butyl-1,2-benzisothiazolin-3-one) used in a 1000 lb formulation is given as 460.02 lbs and the % by weight is given as 46.02%. However, on p. 4 of 19 in MRID 45380902, it is indicated that 460.2 lbs of this component is used in the formulation. The registrant should correct this discrepancy on the CSF. There is a typo on the CSF that should be corrected. In block #10, the third component listed should have a comma after the first numeral 2 rather than a period [redacted]

Data regarding the preliminary analysis of DENSIL DG Fungicide was limited to one batch. OPPTS 830.1700 requires the preliminary analysis of five batches of the product.

The 12-month storage stability testing was performed using high density polyethylene containers, but the specific nature of the commercial packaging used for DENSIL DG Fungicide is not stated. This information should be provided by the registrant.